

# Enterra<sup>®</sup> Therapy System

Humanitarian Device Exemption (HDE) H990014

Pediatric Advisory Committee  
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# Device Description

Enterra is a surgically-implanted gastric electrical stimulator (GES) consisting of the following:

1. A neuro-stimulator placed in a subcutaneous abdominal pocket, which delivers electrical pulses
2. Two intramuscular leads implanted into the stomach greater curvature at the limit of the corpus-antrum
3. An external programmer

## Indications for Use

Enterra is indicated for the treatment of patients with chronic, intractable (drug-refractory) nausea and vomiting secondary to gastroparesis [GP] of diabetic or idiopathic etiology in patients aged 18 to 70 years.



# Annual Distribution Numbers

**The Annual Distribution Number (ADN) is currently defined as the number of devices reasonably needed to treat, diagnose, or cure a population of 8,000 individuals in the U.S.**

- The ADN for Enterra is 4,000 (based on original device approval)

**The number of units sold since the 2016 PAC were:**

- 1,865 neuro-stimulators
- 2,462 leads

**The number of units implanted in 2016 reporting period were 93 total:**

- 56 -first device implants (37 in 18 - 21 years old and 19 in <18 years)
- 37 -as device replacement in pediatric patients

# Medical Device Report (MDR) Review

## Search Criteria (FDA/CDRH Database):

- Report Time Period: May 1, 2016 to April 30, 2017
- Product Code: LNQ (Intestinal Stimulator)
- Brand Name: Enterra

## Search Results:

- 404 Total MDRs\*
- 15 Pediatrics (12 to <22 years)
- 271 Adults ( $\geq$  22 years)
- 118 cases were indeterminate age

# Event Type Distribution by Patient Age

Event Type	Total MDR Count	Pediatric (<22)	Adult (≥22)	No Reported Age (Indeterminate)
Death	2	0	1	1
Injury*	255	13	159	83
Malfunction**	144	2	109	33
<b>Total</b>	<b>401</b>	<b>15</b>	<b>269</b>	<b>117</b>

Three (3) MDRs were excluded since the events were reported in two journal articles in April 2016, which is outside of the defined date range for this analysis

(\*) *“Injury”* (CFR 803.3) includes an event that is life-threatening or results in permanent impairment of a body function or permanent damage to a body structure or necessitates medical or surgical intervention(s) to preclude permanent impairment of a body function or permanent damage to a body structure.

(\*\*) *“Malfunction”* (CFR 803.3) means the failure of a device to meet its performance specifications or otherwise perform as intended; it is reportable when it is likely to cause or contribute to a death or serious injury if the malfunction were to recur.

# Time to Event Occurrence (TTEO)\*

Time to Event Occurrence (TTEO)	Pediatric (<22 y)	Adult (≥22 y)	Indeterminate (No Reported Age)
≤30 days	6	46	2
31 days – 364 days	4	65	8
1 – 5 years ≤ 21-months: All Pediatric pts	5	113	18
>5 years	0	20	7
<b>Totals (N=294)</b>	<b>15</b>	<b>244</b>	<b>35</b>

\* Time to Event Occurrence (TTEO) was calculated as the time between the date of Implant and the date of the Event.

# Adverse Events in Pediatric Patients Year-to-Year Comparison

Adverse Events 5/2015 – 4/2016	Occurrences in MDRs*	Adverse Events 5/2016 – 4/2017	Occurrences in MDRs*
Electric Shock/Nerve Stimulation, Inappropriate Electric Shock	6	Nausea/Vomiting	9
Nausea/Vomiting	4	Pain/Discomfort/ Abdominal Pain	6
Pain/Discomfort/ Abdominal Pain	2	Therapeutic Response Decreased/Paresis	5
Infection/Erosion	2	Infection/Wound Infection	3

(\*) Note: Only the most observed patient problems and issues contained in the narratives of the pediatric MDRs are included. Because a single MDR can contain multiple clinical events, the total number of occurrences in MDRs does not equal the total number of pediatric MDRs.

# MDR Review - Conclusions

- Patient and device problems in Pediatric patients were similar to those observed in adults and indeterminate age
- More MDRs related lead malfunctions or connections (e.g., device impedance issues due to lead connection and/or battery) were reported this year. Manufacturer evaluation of the units was limited due to no device return in 352 of the 401 MDRs
- The reported issues are known inherent risks for the device and do not represent any new safety concern

## Lee S, et al.

*“Some non-FDA approved uses for neuromodulation in treating autonomic nervous system disorders: A Discussion of the preliminary support.”*

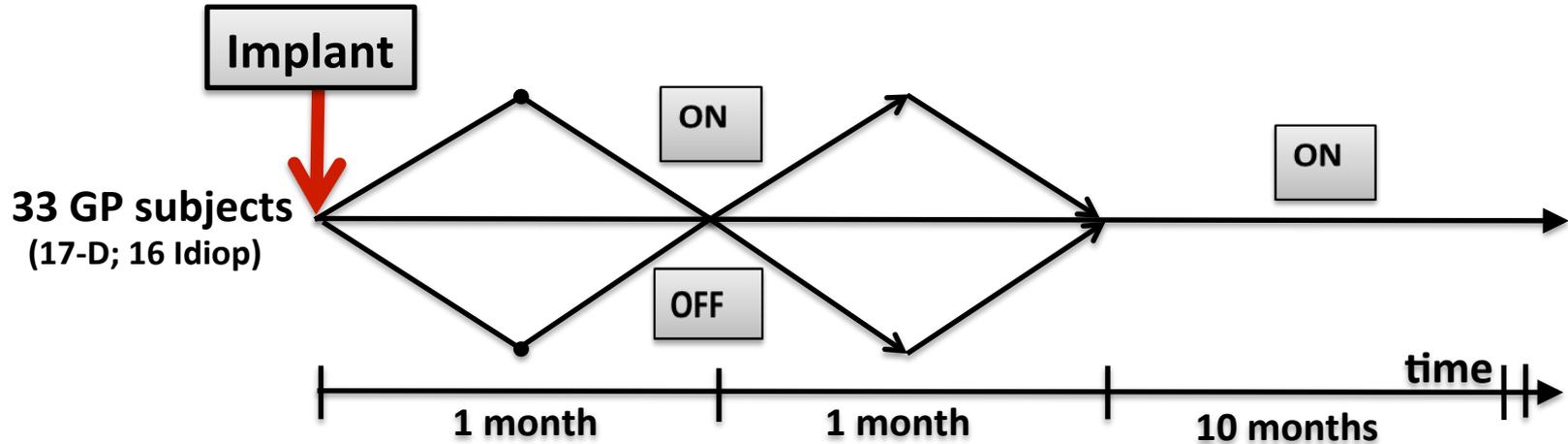
**Neuromodulation 2016, 19:791-803**

### Summary:

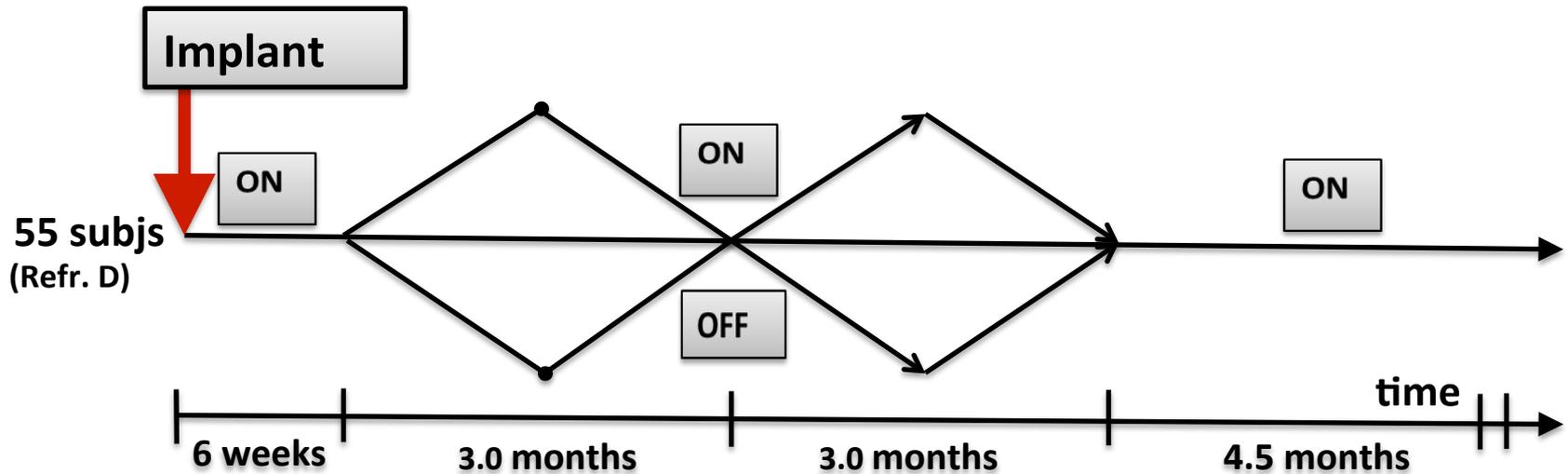
- Systematic literature review on neuromodulation treatment modalities and conditions for autonomic nervous system disorders: Gastric Electrical Stimulation (GES), Gastroparesis(GP), Vagus Nerve Stimulation, Asthma, and others
- The authors identified 4 papers involving results of GES for treatment of GP that met search criteria. Only 2 papers: **Abell et al., and McCallum et al. included Pediatric patients**
- **Abell et al., and McCallum et al.** did not meet the search criteria as they were published in 2003 and 2010, respectively, and included in the previous 2014 PAC meeting.

# Study Design

## Abell et al.



## McCallum et al.



# Abell et al. and McCallum et al. - Results

## Probable Benefits

- Patients in “ON” mode treatment showed a greater reduction in median vomiting frequency than patients in “OFF” mode compared to baseline and study earlier time-points. The highest improvement was observed in the Diabetic cohort compared to Idiopathic and Refractory Diabetic patients
- Improvement in total symptoms and severity scores was also reported
- Gastric emptying time was reported to be modestly accelerated or unchanged

## Safety

- Most commonly reported Patient-related SAEs were: “Hospitalizations” associated with GP symptoms (>32.8% of all patient-related AEs), ketoacidosis, vomiting, hematemesis, hypoglycemia, and hypertension
- Most commonly reported Device-related SAEs were: Device explant and device migration/dislodgment leading to surgical intervention due to site infection, erosion, or hematoma
- Total 7 deaths, -none of them was considered be device or therapy-related

# Literature Review - Conclusions

- Improvement/reduction of upper GI symptoms. Effects on the need for nutritional support was not evaluated. Additional surgery may be required
- Device-related adverse events were consistent with those identified in previous literature reviews and in the product labeling (with exception of hematoma), and do not raise new safety concerns
- Literature review limitations:
  - Only one paper met search criteria
  - Study design issues (e.g., small sample size, short F/u, no data for the Pediatric cohort), and low level scientific evidence
  - Unclear if benefits reported in overall study population represented the Pediatric cohort of patients
- There is limited ability to make firm conclusions about the probable benefits and safety of Enterra in the Pediatric population

# CDRH Recommendations

FDA will continue surveillance and report the following to the PAC in 2018:

- Annual Distribution Numbers
- MDR data
- Literature review results

# Question to the PAC

Does the Committee agree with CDRH's conclusions and recommendations?

# ACKNOWLEDGEMENT

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(\* ) Slides prepared by

